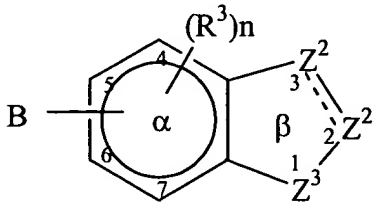
CLAIM AMENDMENTS

a'

1. (currently amended): A compound of the formula:



(1)

and the pharmaceutically acceptable salts thereof, or a pharmaceutical composition thereof, wherein

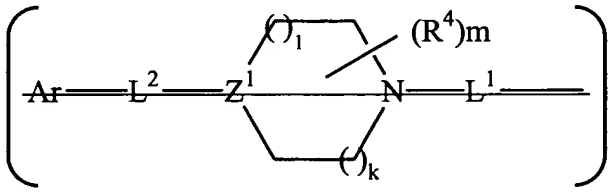
 represents a single or double bond;

B is $-W_i-COX_jY$ wherein Y is COR^2 or an isostere thereof and R^2 is hydrogen or a noninterfering substituent, each of W and X is a spacer of 2-6Å, and each of i and j is independently 0 or 1;

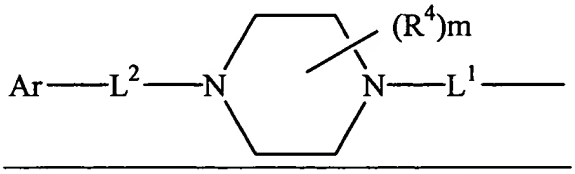
each R^3 is independently a noninterfering substituent, where n is 0-3;

Z^3 is NR^7 or O; wherein R^7 is H or a noninterfering substituent;

one Z^2 is CA or CR^8A and the other is CR^1, CR^1_2, NR^6 or N wherein each R^1, R^6 and R^8 is independently hydrogen or noninterfering substituent; wherein A is:



~~such that Z^1 is CR^5 or N wherein R^5 is hydrogen or a noninterfering substituent; each of l and k is an integer from 0-2 wherein the sum of l and k is 0-3;~~



Ar is an aryl group substituted with 0-5 noninterfering substituents, wherein two noninterfering substituents can form a fused ring;

each R^4 is independently a noninterfering substituent where m is 0-4;

each of L^1 and L^2 is a linker; and

the distance between the atom of Ar linked to L^2 and the center of the β ring is [[4.5-]] no more than 24Å.

a1

2. (original): The compound of claim 1 wherein B is -COXjCOR^2, and

wherein R^2 is H, or is straight or branched chain alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroalkyl, heteroaryl, or heteroarylalkyl, each optionally substituted with halo, alkyl, heteroalkyl, SR, OR, NR_2, OCOR, NRCOR, $NRCONR_2$, $NRSO_2R$, $NRSO_2NR_2$, $OCONR_2$, CN, COOR, $CONR_2$, COR, or R_3Si wherein each R is independently H, alkyl, alkenyl or aryl or the heteroatom-containing forms thereof, or

wherein R^2 is OR, NR_2, SR, $NRCONR_2$, $OCONR_2$, or $NRSO_2NR_2$, wherein each R is independently H, alkyl, alkenyl or aryl or the heteroatom-containing forms thereof, and wherein two R attached to the same atom may form a 3-8 member ring and wherein said ring may further be substituted by alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroalkyl, heteroaryl, heteroarylalkyl, each optionally substituted with halo, SR, OR, NR_2, OCOR, NRCOR, $NRCONR_2$, $NRSO_2R$, $NRSO_2NR_2$, $OCONR_2$, or R_3Si wherein each R is independently H, alkyl, alkenyl or aryl or the heteroatom-containing forms thereof wherein two R attached to the same atom may form a 3-8 member ring, optionally substituted as above defined; and

X, if present, is alkylene.

3. (original): The compound of claim 1 wherein Y is an isostere of COR^2.

4. (original): The compound of claim 3 wherein Y is tetrazole; 1,2,3-triazole; 1,2,4-triazole; or imidazole.

5. (original): The compound of claim 1 wherein each of i and j is 0.

6. (original): The compound of claim 2 wherein j is 0.

7. (original): The compound of claim 1 wherein Z^3 is NR^7.

8. (original): The compound of claim 7 wherein R^7 is H or is optionally substituted alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, or is SOR, SO_2R, RCO, COOR, alkyl-COR, SO_3R, $CONR_2$, SO_2NR_2, CN, CF_3, NR_2, OR, alkyl-SR, alkyl-SOR, alkyl-SO_2R, alkyl-OCOR, alkyl-COOR, alkyl-CN, alkyl-$CONR_2$, or R_3Si, wherein each R is independently H, alkyl, alkenyl or aryl or heteroforms thereof.

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9. (original): The compound of claim 8 wherein R^7 is H, or is optionally substituted alkyl, or acyl.

10. (canceled)

11. (original): The compound of claim 1 wherein L^1 is CO, CHOH or CH_2.

12. (original): The compound of claim 11 wherein L^1 is CO.

13-14. (canceled)

15. (original): The compound of claim 1 wherein L^2 is alkylene (1-4C) or alkenylene (1-4C) optionally substituted with a moiety selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, NH-aroyl, halo, OR, NR_2, SR, SOR, SO_2R, OCOR, NRCOR, $NRCONR_2$, NRCOOR, $OCONR_2$, RCO, COOR, alkyl-OOR, SO_3R, $CONR_2$, SO_2NR_2, $NRSO_2NR_2$, CN, CF_3, R_3Si, and NO_2, wherein each R is independently H, alkyl, alkenyl or aryl or heteroforms thereof, and wherein two substituents on L^2 can be joined to form a non-aromatic saturated or unsaturated ring that includes 0-3 heteroatoms which are O, S and/or N and which contains 3 to 8 members or said two substituents can be joined to form a carbonyl moiety or an oxime, oximeether, oximeester or ketal of said carbonyl moiety.

16. (original): The compound of claim 15 wherein L^2 is unsubstituted alkylene.

17. (original): The compound of claim 15 wherein L^2 is unsubstituted methylene, methylene substituted with alkyl, or -CH=.

18. (original): The compound of claim 1 wherein Ar is optionally substituted with 0-5 substituents selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, NH-aroyl, halo, OR, NR_2, SR, SOR, SO_2R, OCOR, NRCOR, $NRCONR_2$, NRCOOR, $OCONR_2$, RCO, COOR, alkyl-OOR, SO_3R, $CONR_2$, SO_2NR_2, $NRSO_2NR_2$, CN, CF_3, R_3Si, and NO_2, wherein each R is independently H, alkyl, alkenyl or aryl or heteroforms thereof, and wherein two of said optional substituents on adjacent positions can be joined to form a fused, optionally substituted aromatic or nonaromatic, saturated or unsaturated ring which contains 3-8 members.

19. (original): The compound of claim 18 wherein Ar is optionally substituted phenyl.

20. (original): The compound of claim 19 wherein said optional substitution is by halo, OR, or alkyl.

21. (original): The compound of claim 20 wherein said phenyl is unsubstituted or has a single substituent.

22. (original): The compound of claim 1 wherein R^4 is selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, NH-aroyl, halo, OR, NR_2, SR, SOR, SO_2R, OCOR, NRCOR, $NRCONR_2$, NRCOOR, $OCONR_2$, RCO, COOR, alkyl-OOR, SO_3R, $CONR_2$, SO_2NR_2, $NRSO_2NR_2$, CN, CF_3, R_3Si, and NO_2, wherein each R is independently H, alkyl, alkenyl or aryl or heteroforms thereof and two of R^4 on adjacent positions can be joined to form a fused, optionally substituted aromatic or nonaromatic, saturated or unsaturated ring which contains 3-8 members, or R^4 is =O or an oxime, oximeether, oximeester or ketal thereof.

23. (original): The compound of claim 22 wherein each R^4 is halo, OR, or alkyl.

24. (original): The compound of claim 23 wherein m is 0, 1, or 2.

25. (original): The compound of claim 24 wherein m is 2 and both R^4 are alkyl.

a1

26. (original): The compound of claim 1 wherein each R^3 is halo, alkyl, heteroalkyl, OCOR, OR, NRCOR, SR, or NR_2, wherein R is H, alkyl, aryl, or heteroforms thereof.

27. (original): The compound of claim 26 wherein R^3 is halo or alkoxy.

28. (original): The compound of claim 27 wherein n is 0, 1 or 2.

29. (original): The compound of claim 1 wherein L^1 is coupled to the β ring at the 5-position.

30. (original): The compound of claim 1 wherein Z^2 at position 3 is CA or CH^1A.

31. (original): The compound of claim 30 wherein the Z^2 at position 2 is CR^1 or CR^1_2.

32. (original): The compound of claim 31 wherein R^1 is hydrogen, or is alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, NH-aroyl, halo, OR, NR_2, SR, SOR, SO_2R, OCOR, NRCOR, $NRCONR_2$, NRCOOR, $OCONR_2$, RCO, COOR, alkyl-OOR, SO_3R, $CONR_2$, SO_2NR_2, $NRSO_2NR_2$, CN, CF_3, R_3Si, and NO_2, wherein each R is independently H, alkyl, alkenyl or aryl or heteroforms thereof and two of R^1 can be joined to form a fused, optionally substituted aromatic or nonaromatic, saturated or unsaturated ring which contains 3-8 members.

33. (original): The compound of claim 32 wherein each R^1 is selected from the group consisting of H, alkyl, acyl, aryl, arylalkyl, heteroalkyl, heteroaryl, halo, OR, NR_2, SR, NRCOR, alkyl-OOR, RCO, COOR, and CN, wherein each R is independently H, alkyl, or aryl or heteroforms thereof.

34. (original): The compound of claim 30 wherein Z^2 at position 2 is N or NR^6.

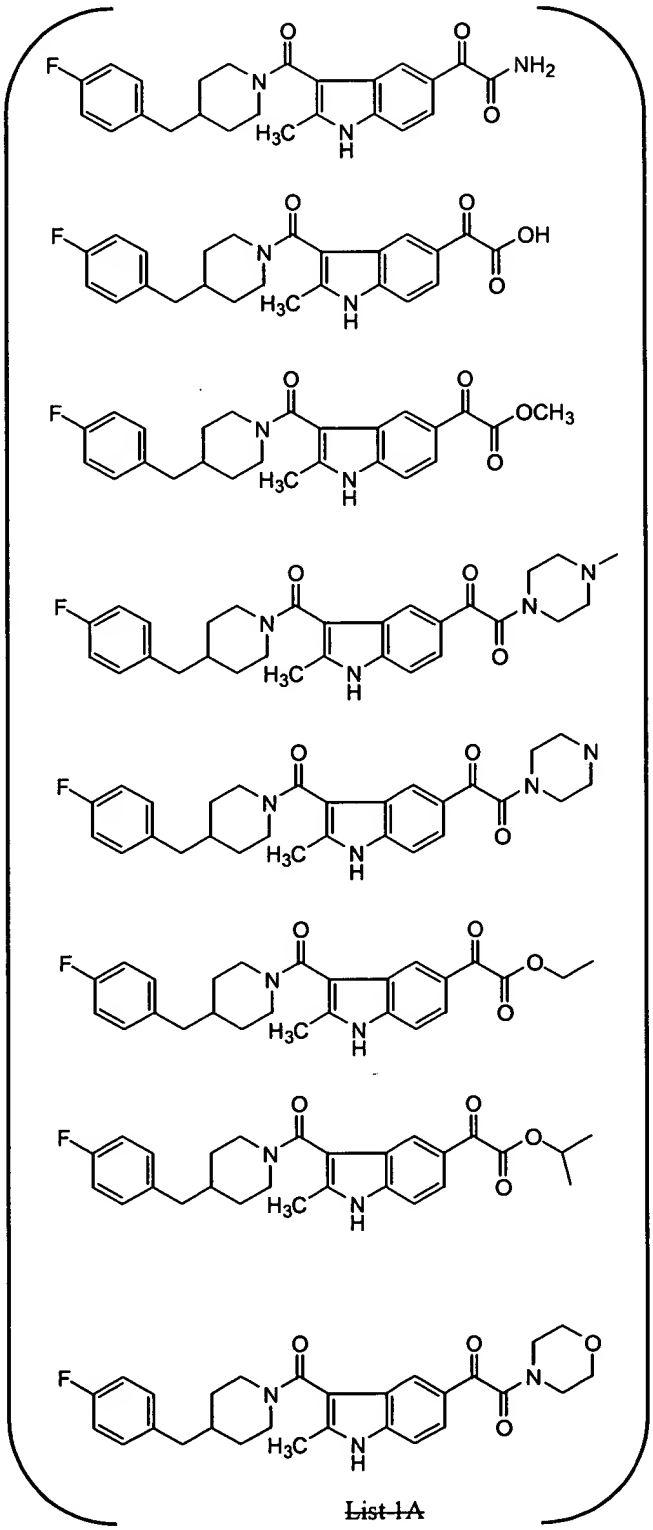
35. (original): The compound of claim 34 wherein R^6 is H, or alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, or is SOR, SO_2R, RCO, COOR, alkyl-COR, SO_3R, $CONR_2$, SO_2NR_2, CN, CF_3, or R_3Si wherein each R is independently H, alkyl, alkenyl or aryl or heteroforms thereof.

36. (original): The compound of claim 1 wherein  represents a double bond.

37. (original): The compound of claim 1 wherein the distance between the atom on Ar linked to L^2 and the center of the β ring is 7.5-11Å.

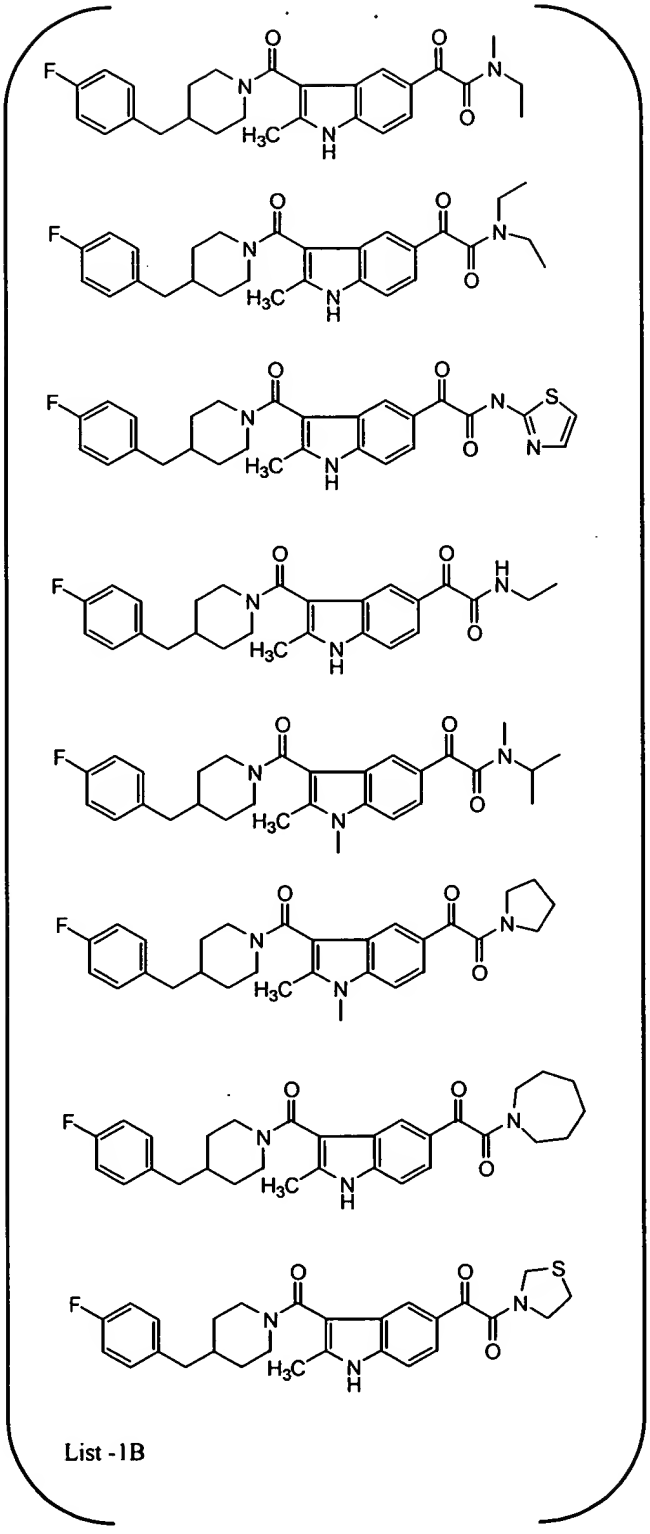
38. (original): The compound of claim 1 wherein the compound of formula (1) is selected from the group consisting of:

Q1



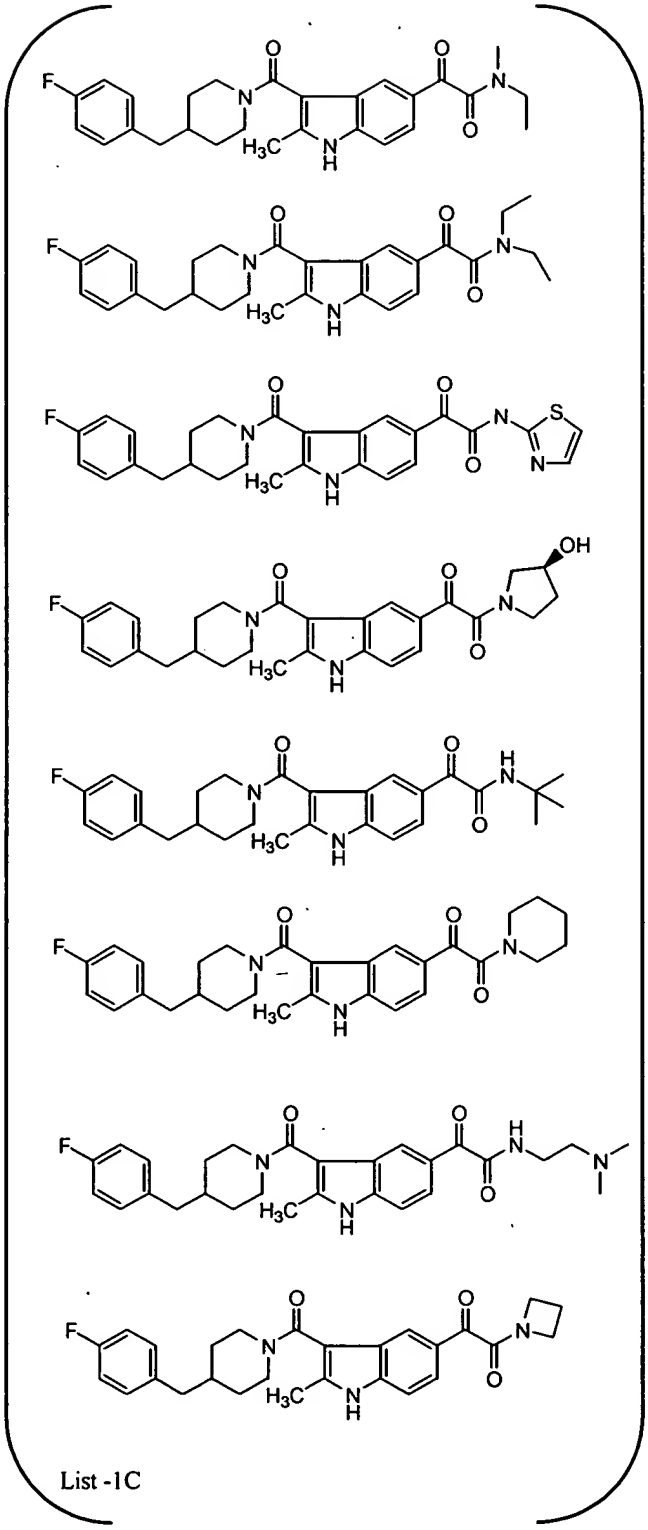
~~List 1A~~

a'



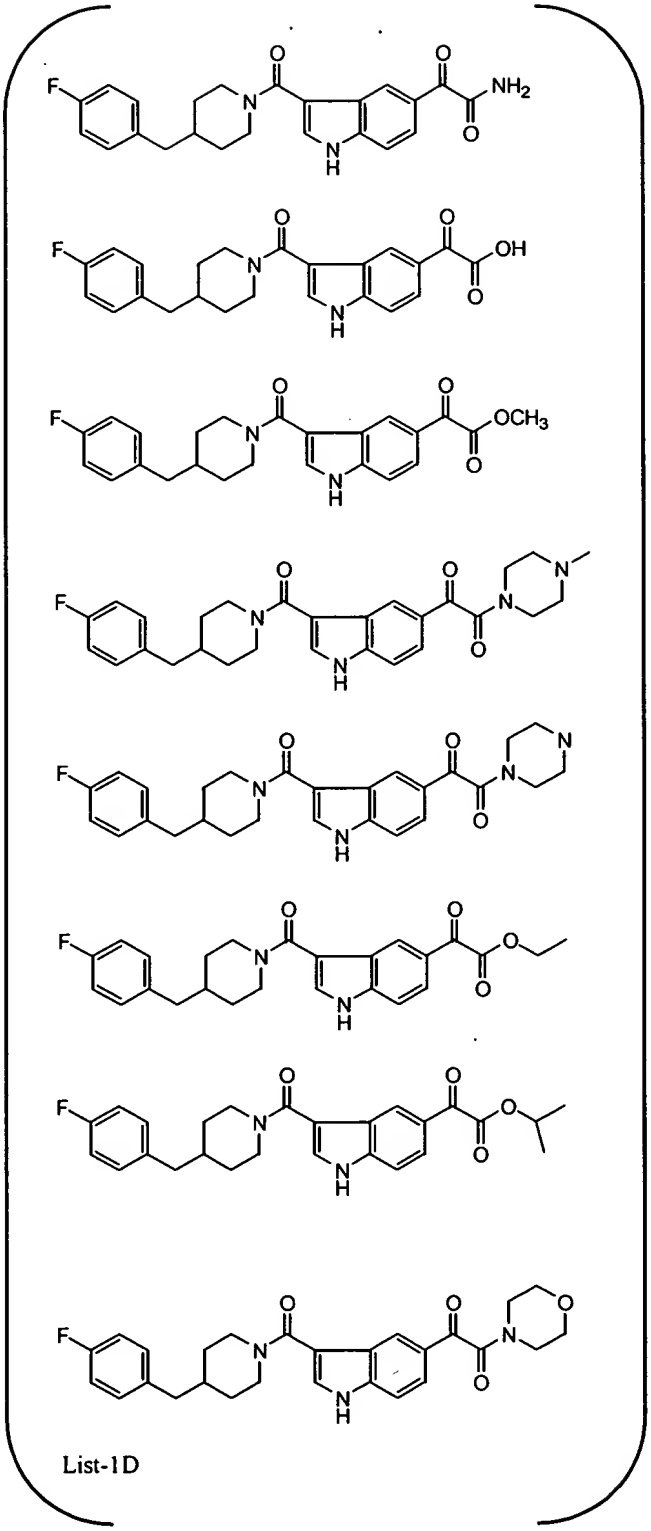
List -1B

Q1



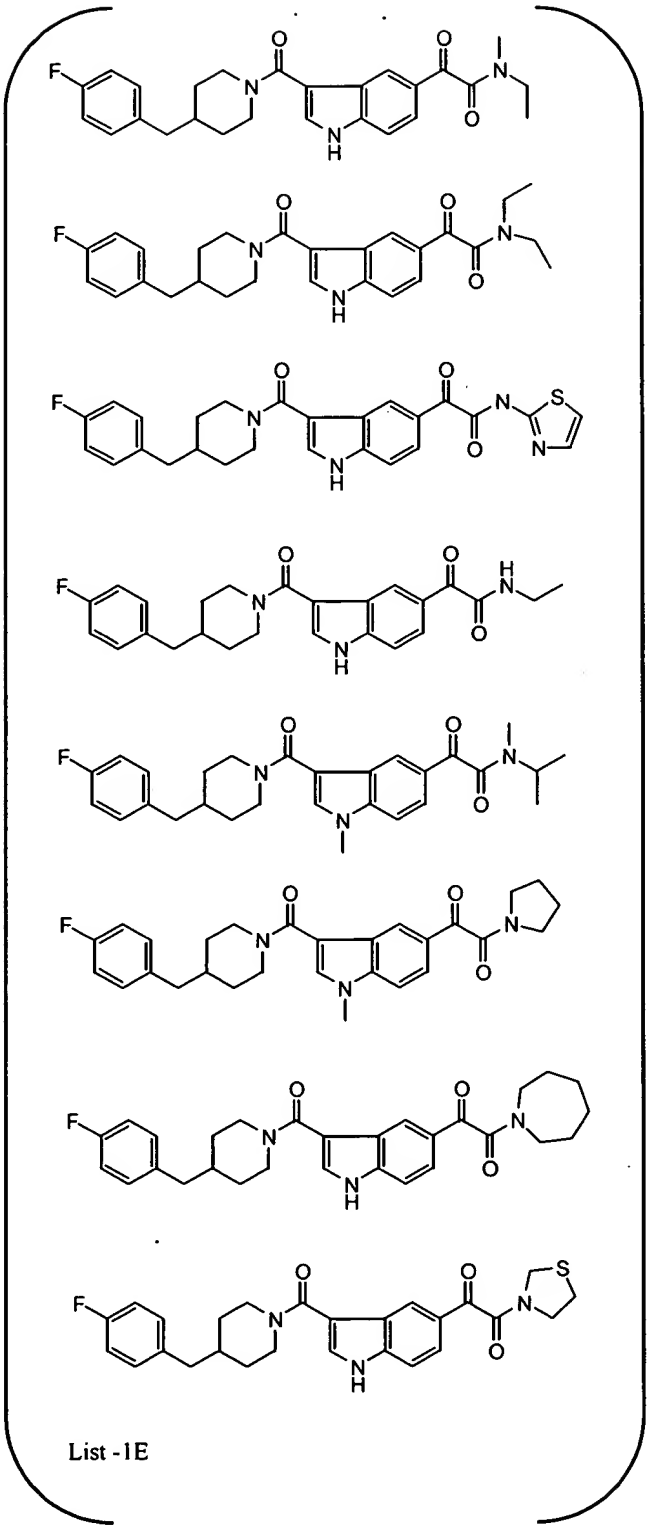
List -1C

a'



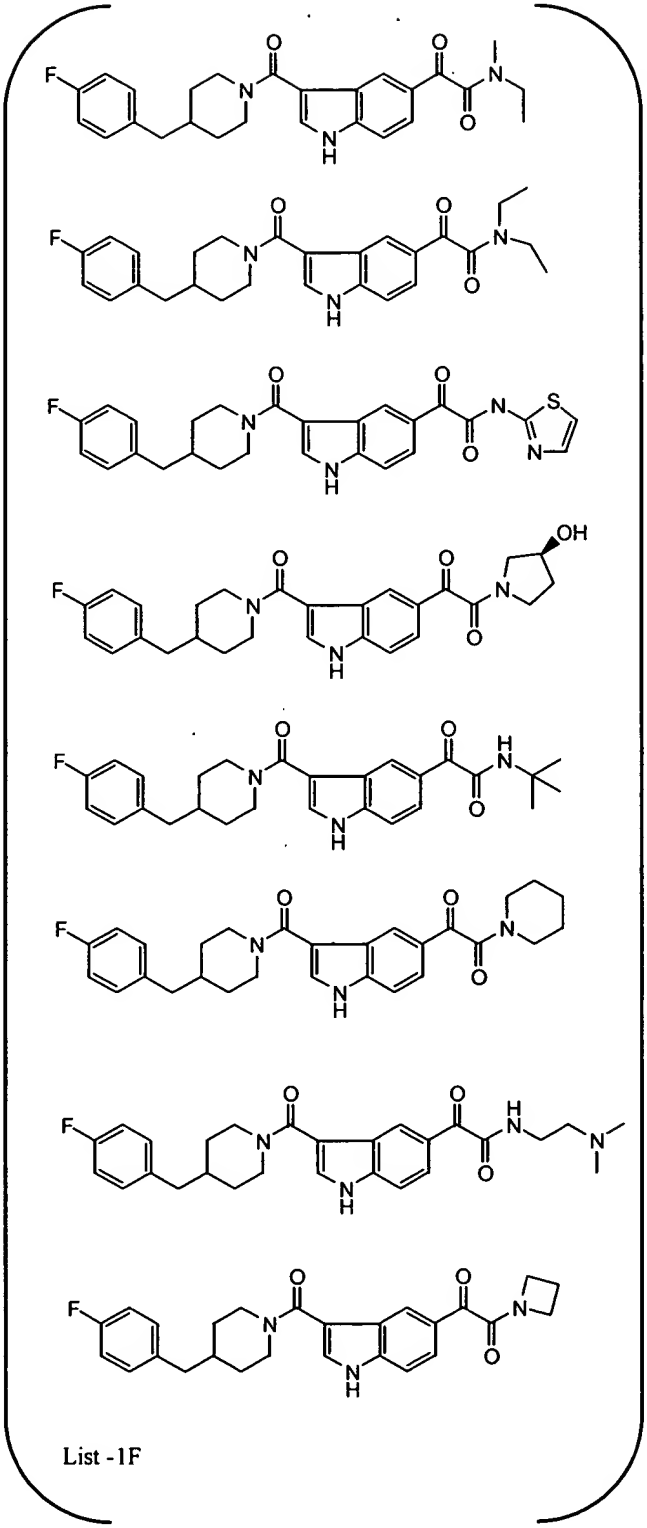
List-1D

a1



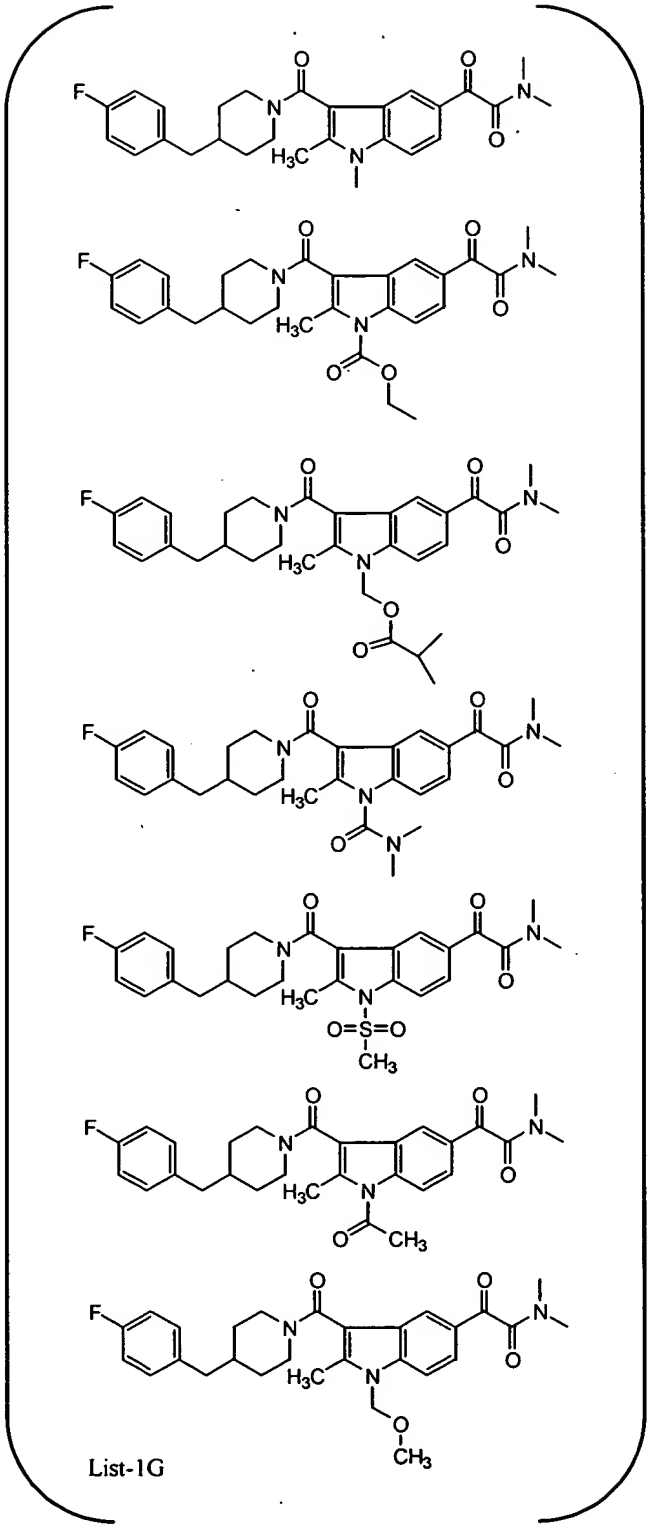
List -1E

a1



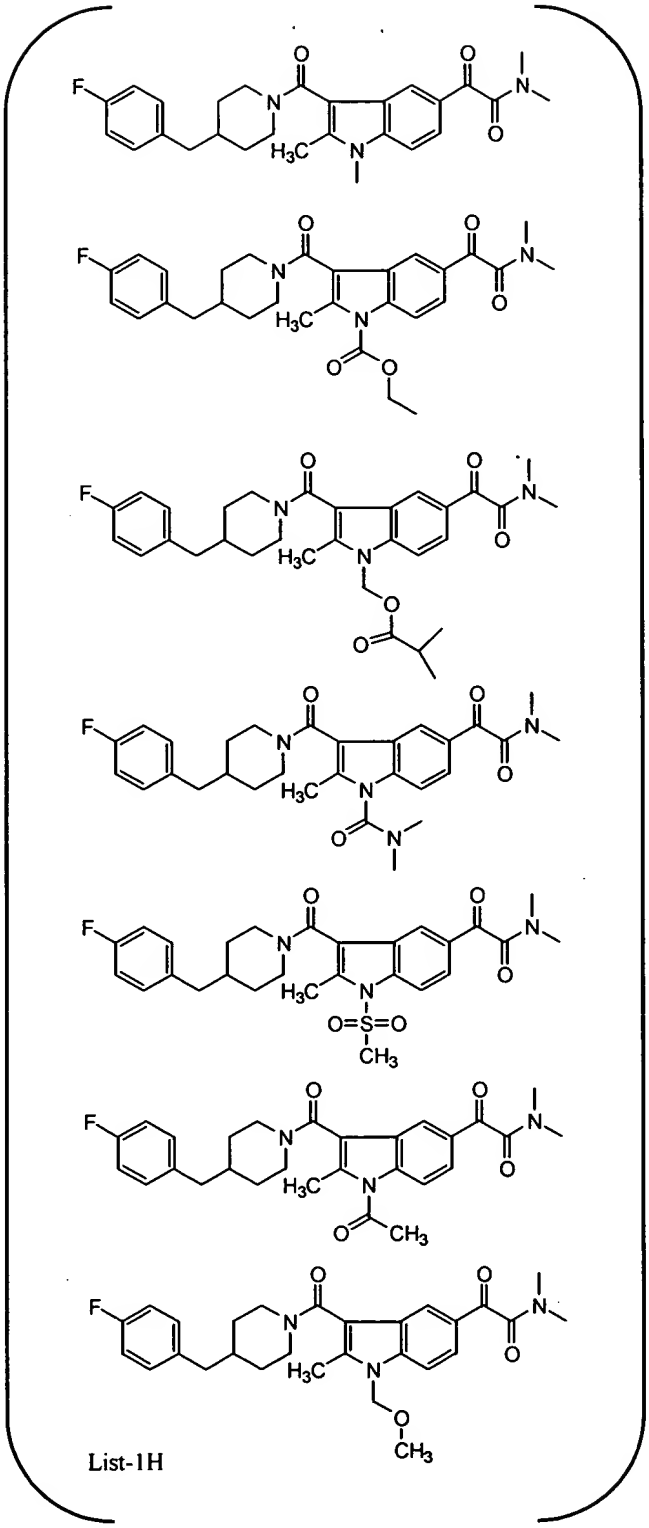
List -1F

a'



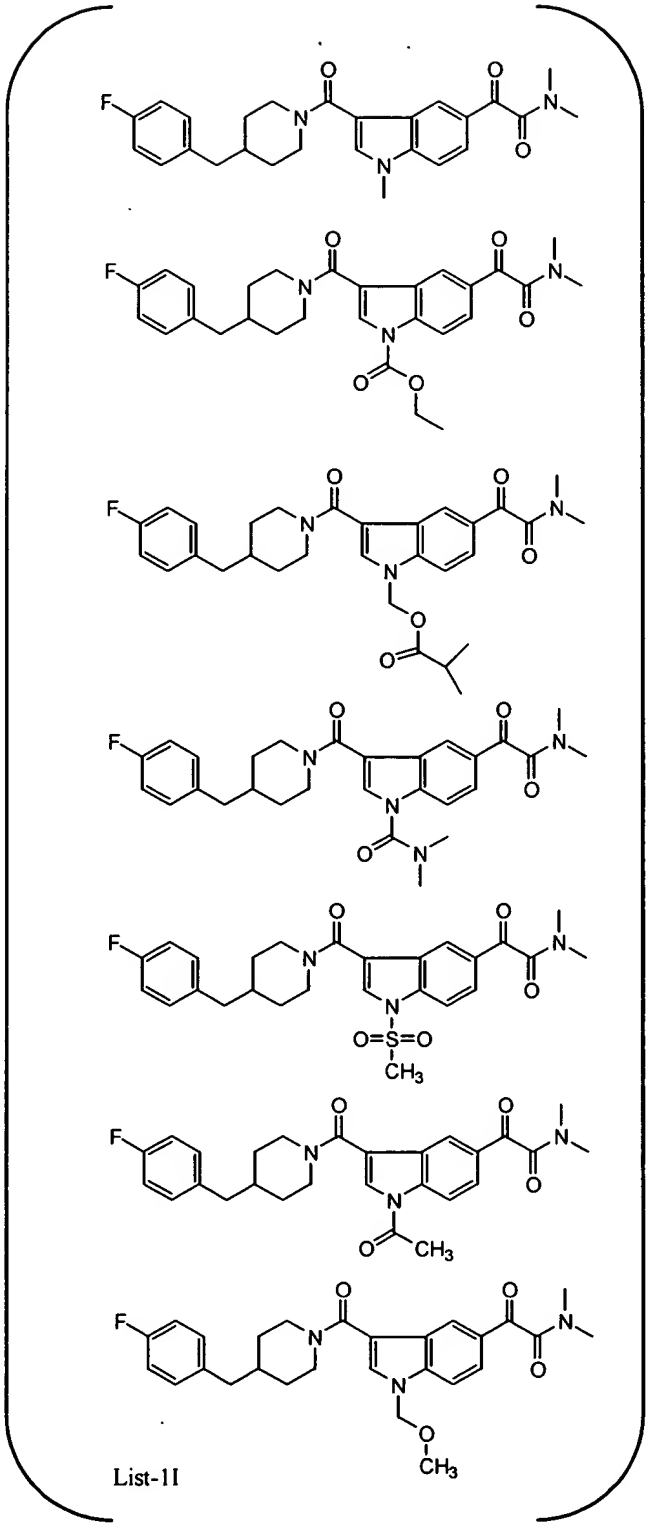
List-1G

91



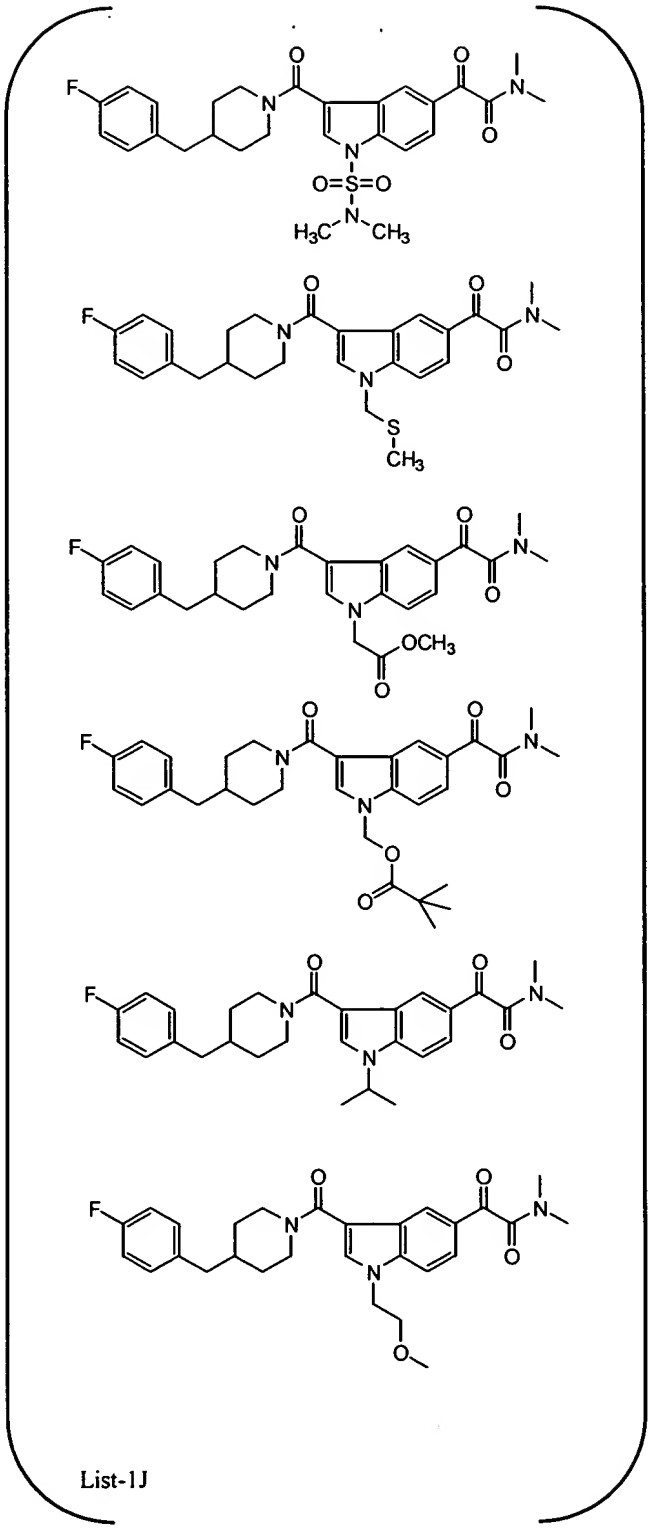
List-1H

q'



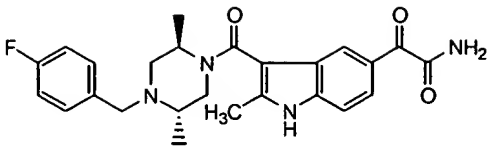
List-1I

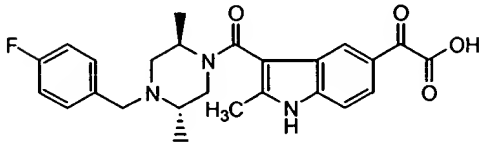
Q1

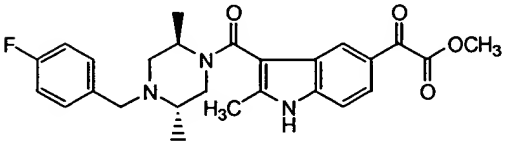


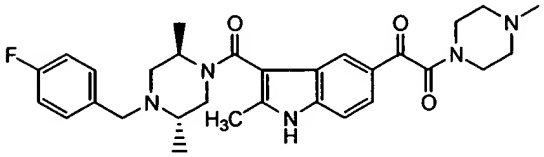
List-1J

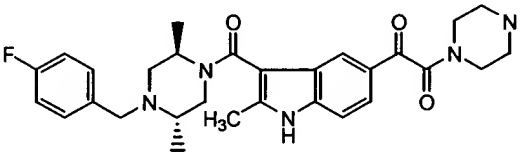
a'

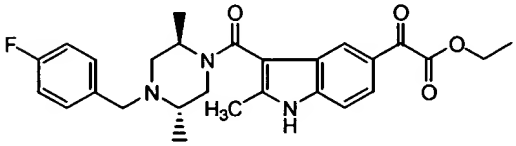


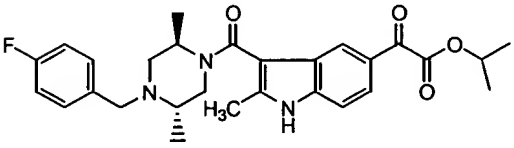


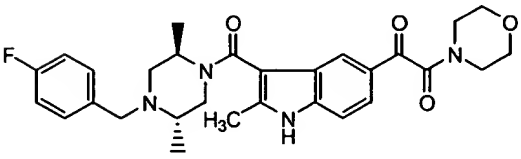






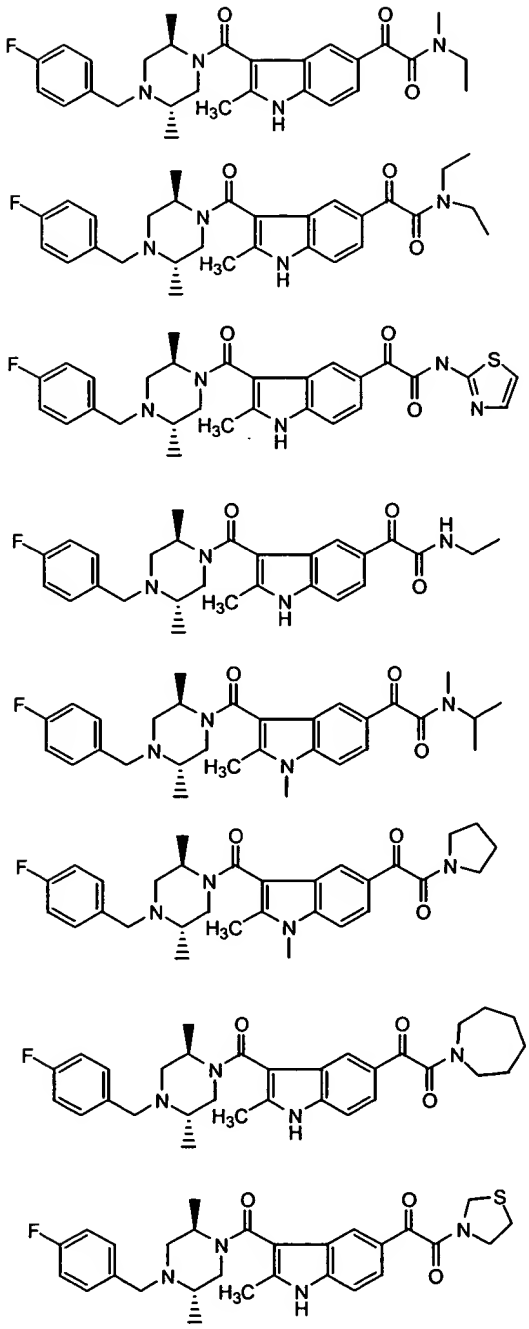






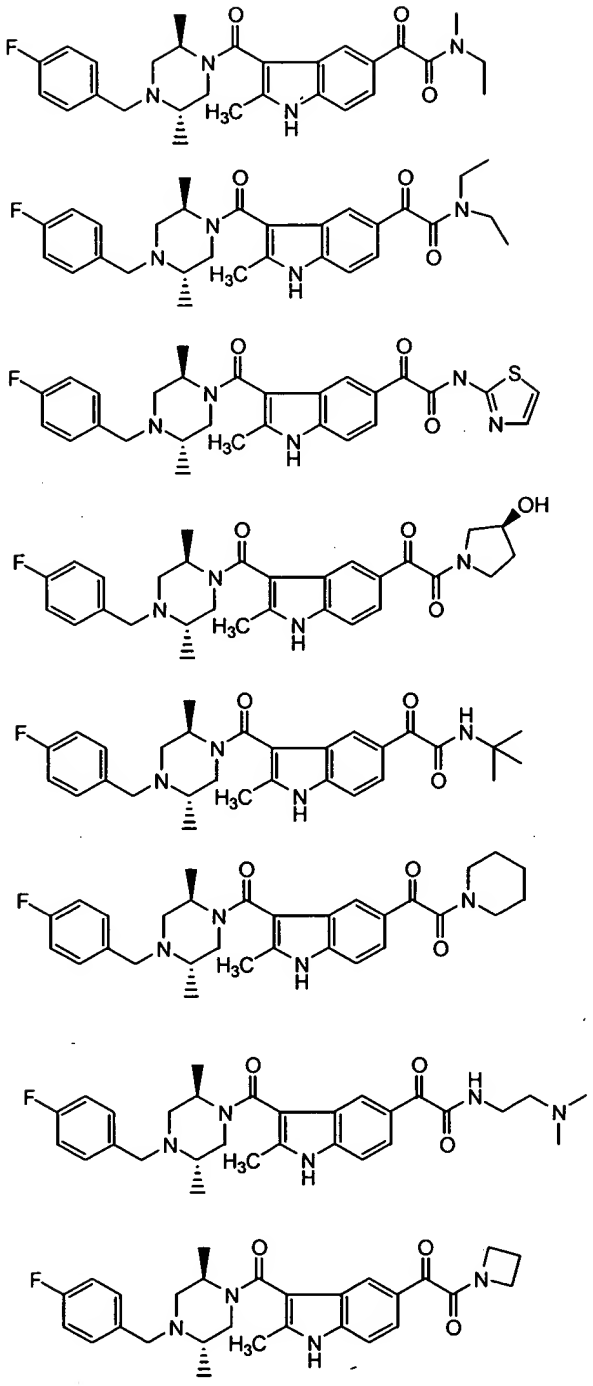
List-2A

Q1



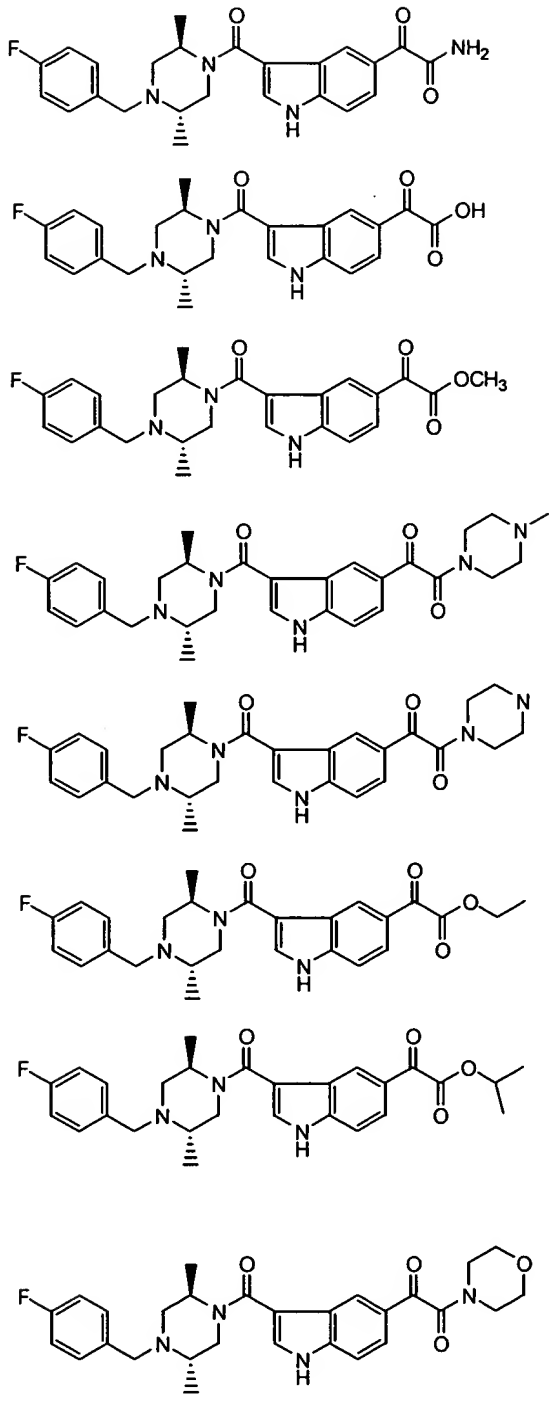
List -2B

a'



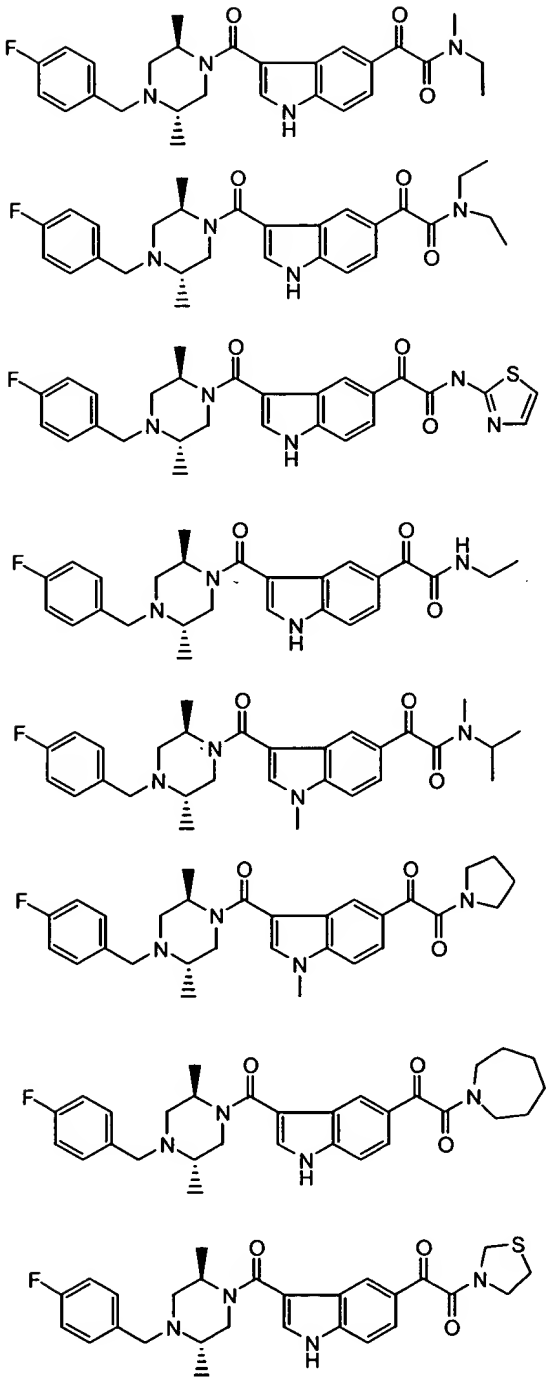
List -2C

a'



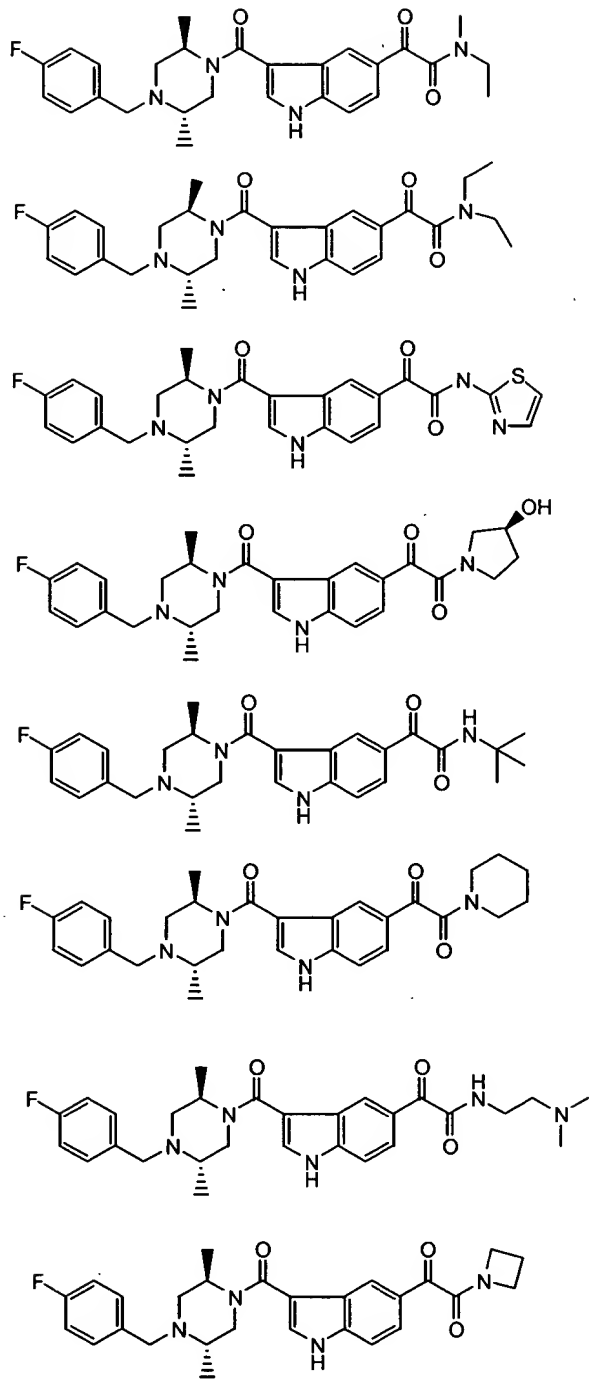
List-2D

a'



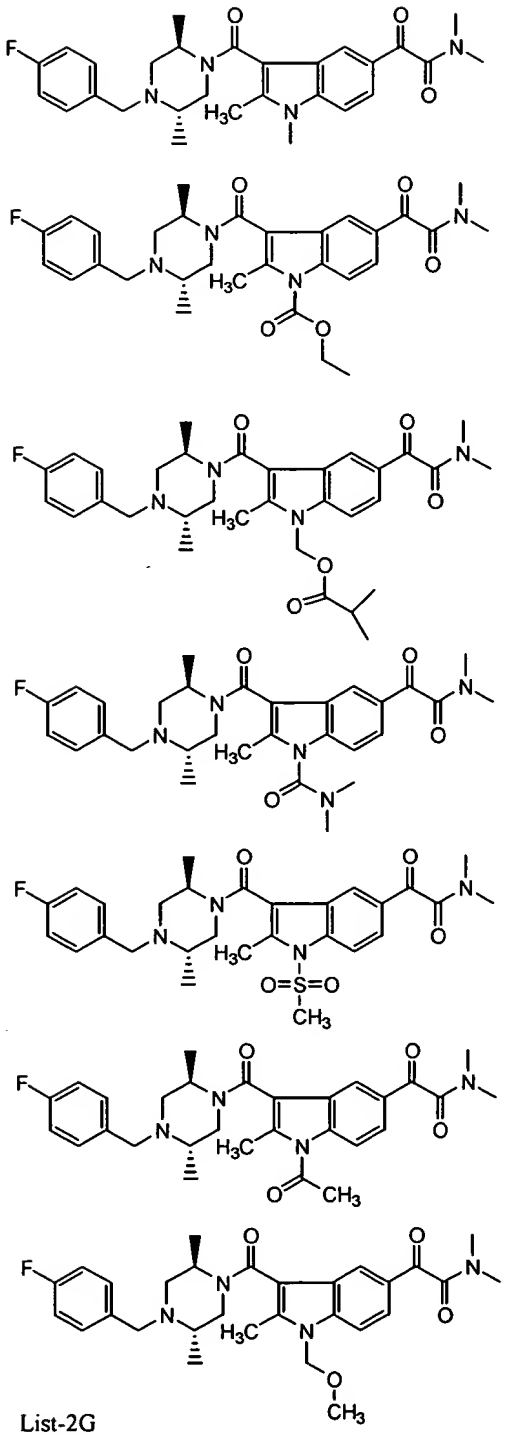
List -2E

a'



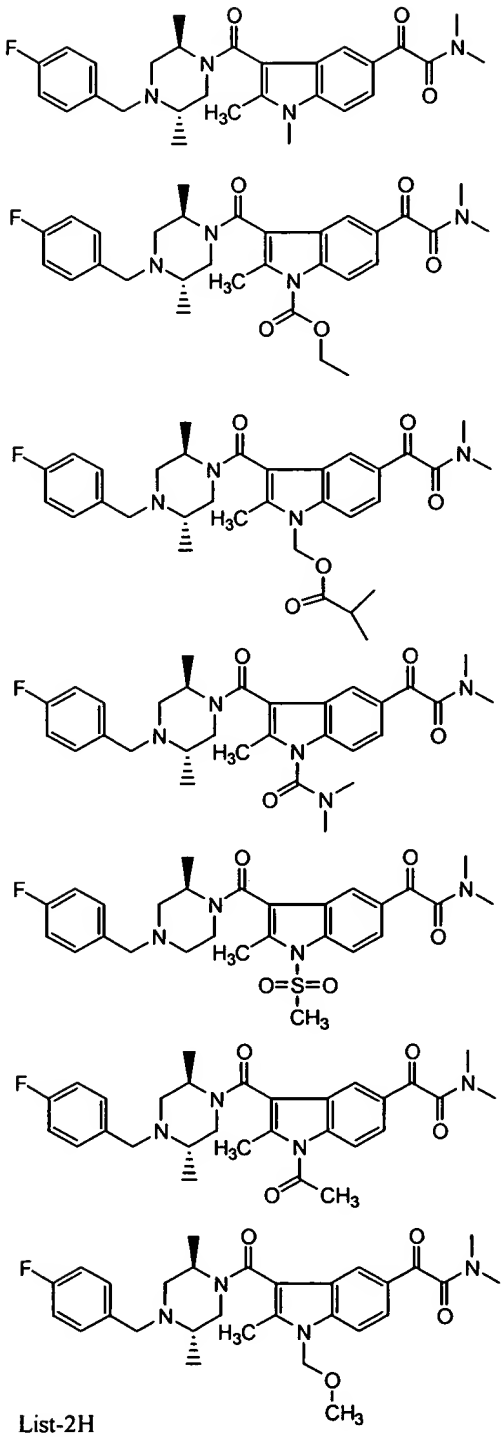
List -2F

Q1



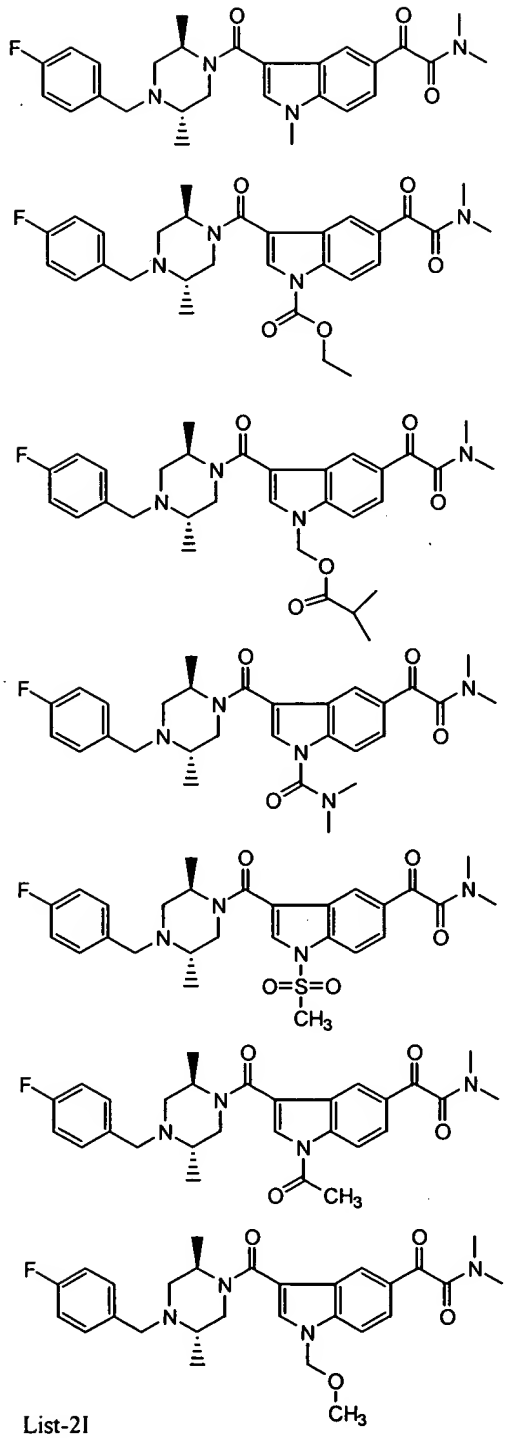
List-2G

a1



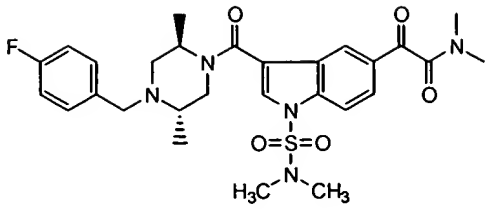
List-2H

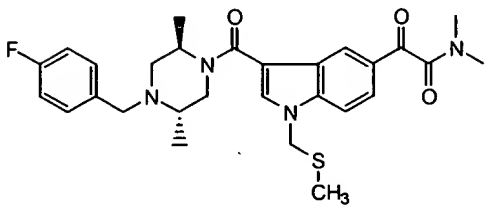
a1

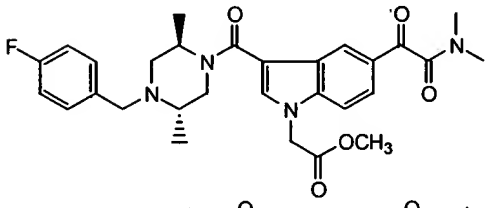


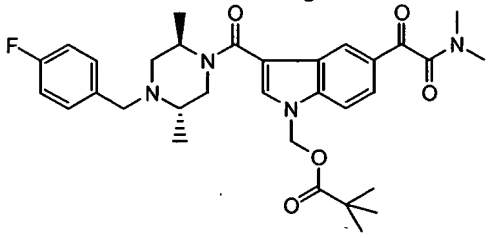
List-2I

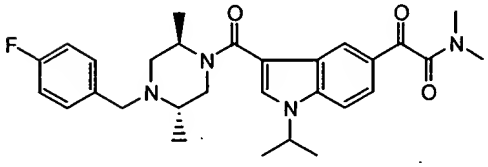
a'

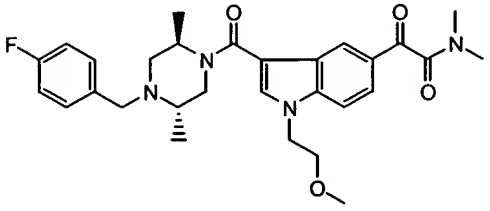








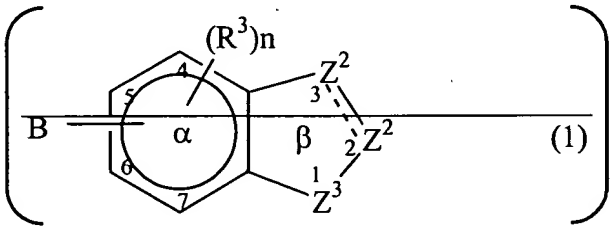




List-2J

39. (currently amended): A pharmaceutical composition ~~for treating conditions characterized by enhanced p38-α activity~~ which composition comprises

a therapeutically effective amount of [[a]] the compound of ~~the formula~~ claim 1 or a



~~and the~~ pharmaceutically acceptable [[salts]] salt thereof in admixture with at least one pharmaceutically acceptable carrier ~~, or a pharmaceutical composition thereof, wherein~~

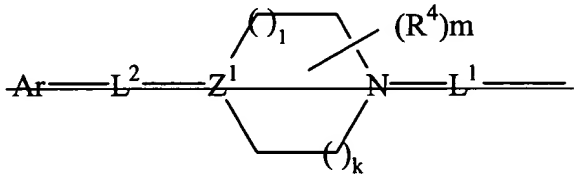
~~represents a single or double bond;~~

~~B is W_i-COX_jY wherein Y is COR^2 or an isostere thereof and R^2 is hydrogen or a noninterfering substituent, each of W and X is a spacer of 2-6Å, and each of i and j is independently 0 or 1;~~

~~each R^3 is independently a noninterfering substituent, where n is 0-3;~~

~~Z^3 is NR^7 or O; wherein R^7 is H or a noninterfering substituent;~~

~~one Z^2 is CA or CR^8A and the other is CR^1, CR^1_2, NR^6 or N wherein each R^1, R^6 and R^8 is independently hydrogen or noninterfering substituent; wherein A is:~~



~~such that Z^1 is CR^5 or N wherein R^5 is hydrogen or a noninterfering substituent;~~

~~each of l and k is an integer from 0-2 wherein the sum of l and k is 0-3;~~

~~Ar is an aryl group substituted with 0-5 noninterfering substituents, wherein two noninterfering substituents can form a fused ring;~~

~~each R^4 is independently a noninterfering substituent where m is 0-4;~~

~~each of L^1 and L^2 is a linker; and~~

~~the distance between the atom of Ar linked to L^2 and the center of the β ring is 4.5-24Å.~~

40. (original): The composition of claim 39 which further contains an additional therapeutic agent.

41. (original): The composition of claim 40 wherein said additional therapeutic agent is a corticosteroid, a monoclonal antibody, or an inhibitor of cell division.

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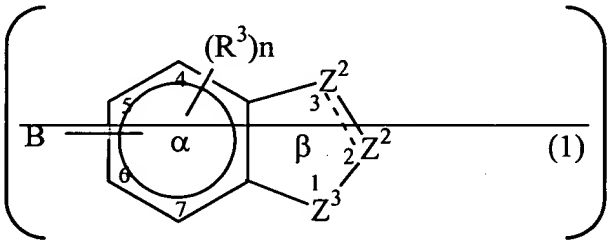
42. (currently amended): A method to treat a condition mediated by p38-α kinase comprising administering to a subject in need of such treatment a compound of ~~the formula~~ claim 1 or:



~~and the~~ a pharmaceutically acceptable [[salts]] salt thereof, or a pharmaceutical composition thereof~~, wherein~~

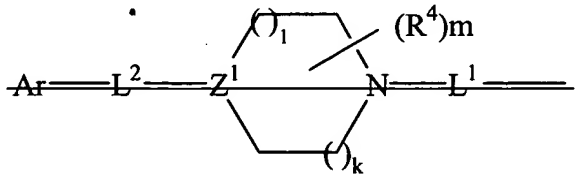
~~represents a single or double bond;~~

~~B is W_i-COX_jY wherein Y is COR^2 or an isostere thereof and R^2 is hydrogen or a noninterfering substituent, each of W and X is a spacer of 2-6Å, and each of i and j is independently 0 or 1;~~

~~each R^3 is independently a noninterfering substituent, where n is 0-3;~~

~~Z^3 is NR^7 or O; wherein R^7 is H or a noninterfering substituent;~~

~~one Z^2 is CA or CR^8A and the other is CR^1, CR^1_2, NR^6 or N wherein each R^1, R^6 and R^8 is independently hydrogen or noninterfering substituent; wherein A is:~~



~~such that Z^1 is CR^5 or N wherein R^5 is hydrogen or a noninterfering substituent;~~

~~each of l and k is an integer from 0-2 wherein the sum of l and k is 0-3;~~

~~Ar is an aryl group substituted with 0-5 noninterfering substituents, wherein two noninterfering substituents can form a fused ring;~~

~~each R^4 is independently a noninterfering substituent where m is 0-4;~~

~~each of L^1 and L^2 is a linker; and~~

~~the distance between the atom of Ar linked to L^2 and the center of the β ring is 4.5-24Å.~~

43. (original): The method of claim 42 wherein said condition is a proinflammation response.

Q1

44. (currently amended): The method of claim 43 wherein said proinflammation response is multiple sclerosis, IBD, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, gouty arthritis, other arthritic conditions, sepsis, ~~septic shock,~~ endotoxic shock, Gram-negative sepsis, toxic shock syndrome, asthma, adult respiratory distress syndrome, ~~stroke,~~ reperfusion injury, ~~CNS injury,~~ psoriasis, restenosis, cerebral malaria, chronic pulmonary inflammatory disease, silicosis, pulmonary sarcosis, a bone resorption disease, graft-versus-host reaction, Crohn's Disease, ulcerative colitis, Alzheimer's or pyresis.